REMARKS

Claims 1-5, 13, and 16-29 are pending. Claims 1-5 and 13 are rejected. Claim 1 is amended. The amendments to claim 1 find support in the specification as originally filed at page 38, lines 3-4 and page 7, line 30 to page 8, line 23. No new matter is added.

Objections to the Specification

The Office Action states that the specification fails to comply with the requirements of 37 C.F.R. §1.821-1.825 relating to the disclosure of amino acid and nucleic acid sequences. The Office Action states that the application contains sequences (Figure 8) that are not included in a sequence listing and are not identified by sequence identifier numbers. Applicants are amending the Brief Description of Figure 8 to make reference to the sequence identifier numbers that have been added to the Substitute Sequence Listing filed herewith. Accordingly, Applicants request that the objections be reconsidered and withdrawn.

Rejection of Claims 1-5 and 13 Under 35 U.S.C. §112, First Paragraph

Enablement

The Office Action states that claims 1-5 and 13 are rejected under §112, first paragraph as allegedly failing to comply with the enablement requirement. The Office Action states that the claims are not enabled for the full scope of the claimed method. The Office Action states that it would require a "great amount" of experimentation to practice the claimed invention, and states further that the prior art references Francis et al. and Kinnunen et al. support the Examiner's assertion that the claimed invention is unpredictable. Applicants disagree and traverse the rejection.

The Examiner has maintained the enablement objection and in particular refers to Francis *et al.,* (2005) Current Opinion in Allergy and Clinical Immunology 5, 537-543. The Examiner has focused on sections of this paper which allegedly refer to potential difficulties in immunotherapy. However it is submitted that these potential

difficulties do not fairly reflect the art as a whole, and cannot be used to conclude that the present application is not enabled.

It is well settled that the termination of enablement is based on the evidence as a whole. MPEP §2164.05. If the entirety of Francis *et al.* is considered then it is noted that the authors make very positive comments concerning peptide based tolerisation. In particular, the concluding paragraph shows that the authors consider use of short synthetic peptides as being capable of improving symptoms and improving patients' ability to tolerate allergen exposure, and essentially that peptide therapy is capable of inducing regulatory T cells that can suppress allergen-specific immune responses. Further the paragraph entitled "Purpose of Review" in the abstract of the paper highlights that peptides have the potential to inhibit T cell function but not induce anaphylaxis. Thus we disagree with the Examiner's reading of Francis *et al.*, and instead believe that this paper shows that peptide immunotherapy is effective.

The Examiner has also focused on Kinnunen *et al.* and stats that this document is relevant because use of altered peptide ligands as described in Kinnunen *et al.*, would also be covered by the present claims. However, amended claim 1 requires the peptide to induce a late phase response during the method of desensitisation, and thus only covers use of peptides which are effective, i.e. which are capable of being presented by the MHC Class II molecules present in the patient and of stimulating the necessary late phase response. The Examiner has referred to page 7 left hand column, second paragraph of this document which refer to disease exacerbation that was observed in a trial of MS. However, this paragraph also notes that activation of allergen-specific T cells has been shown to precede development of tolerance in immunotherapy. Therefore Kinnunen *et al.* draws a distinction between therapy of autoimmune disease and therapy of allergy. This distinction is further discussed in the third paragraph of the same column which makes it clear that potential problems with peptide therapy for autoimmune disease are much less likely to occur peptide therapy for allergy. Therefore Kinnunen *et al.* provides no firm reasons to assume that immunotherapy using peptides would not be effective for allergy.

It is submitted that in referring to portions of specific documents to support objections of enablement, the Office Action does not consider the art as a whole and has not given a fair weight to other disclosure in the same documents or in the documents filed with Applicants' previous response that show that peptide immunotherapy is successful in treatment of allergic disease. When teaching across the art is looked at, it can be concluded that use of peptides to tolerise against allergens has been successful.

The Examiner also notes that the specification does not describe use of non-Fel d-I derived peptides to desensitise patients. However it is not necessary for the specification to describe each and every peptide which could be used in the method of claim 1 as long as such peptides could be obtained by the skilled person by routine means available in the art or with the aid of the teaching in the specification. Again, Applicants note that the law is clear that a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed. MPEP §2164.06. It would be a routine matter for the skilled person to identify suitable peptides that contained MHC Class II epitopes. The specification provides the sequence for numerous examples of allergens that can be used according to the claimed invention. Examples 5 and 6 of the specification show how epitopes can be identified, for example by using binding studies with MHC molecules or by using peptides to stimulate proliferation of T cells. Such techniques would be considered routine in the art, and thus the skilled person would be able to identify suitable peptides for use in the method of claim 1 for any allergen.

In maintaining the rejection, the Office Action acknowledges that one of skill in the art could perform experimentation to identify allergens and peptides with the claimed functional characteristics, but appears to conclude that the enablement requirement is not satisfied because it would be more than routine experimentation to "determine the MHC restriction of every peptide of 5-50 amino acids of any allergen." Again, the quantity of experimentation is not determinative of enablement, particularly when such experimentation is routine and the specification provides, as in this case,

ample teachings to guide the experimentation. In addition, the statement in the Office Action that one of skill in the art would have to "determine the MHC restriction of every 5-50 amino acids of any allergen" in order to practice the invention mischaracterizes the enablement analysis. Given the teachings in the specification and the level of skill in the art, the skilled artisan could routinely determine whether a given peptide antigen could be used in accordance with the claimed invention. The enablement requirement does not necessitate the specification to teach how to make and use every possible variant of the claimed invention. See, e.g., Chiron Corp. v. Genentech, Inc., 363 F.3d 1247 (Fed. Cir. 2004). Accordingly, the specification does enable the invention and Applicants request that the rejection be reconsidered and withdrawn.

Written Description

The Office Action states that claims 1-5 and 13 are rejected for alleged failure to satisfy the written description requirement. The Office Action states that the specification does not adequately describe the full scope of the claimed invention because the specification does not sufficiently teach a correlation between function (desensitization) and structure responsible for desensitization such that one of ordinary skilled in the art would have known which peptides could be generated to have the required function. Applicants disagree and traverse the rejection.

The specification makes it clear that the peptide must have a specific length and must comprise a sequence that demonstrates restriction to a MHC class II molecule; that is, it must be capable of binding to a MHC Class II molecule possessed by the patient. As shown above, the skilled person can ascertain by routine means whether a peptide is capable of binding to a MHC Class II molecule. Thus the specification describes all of the structural requirements that a peptide must have in order to be capable of being used in the method of claim 1. As stated in Applicants' last response, a common desensitization mechanism exists that can be used to tolerise against an allergen that contains a sequence that demonstrates restriction to a MHC class II molecule. Thus, the structure of a peptide allergen that allows it to bind to an MCH class II molecule correlates with the function of tolerising against that allergen.

Accordingly, the specification, in combination with the knowledge and skill in the art provides ample teachings to evidence to one of skill in the art that Applicants were in possession of the full scope of the claimed invention as of the instant filing date. Applicants, therefore, request that the rejection be reconsidered and withdrawn.

Rejection of Claims 1-5 and 13 Under 35 U.S.C. §102(b)

WO94/24281

The Office Action states that the claims are rejected as anticipated by WO 94/24281. The Office Action states that the '281 PCT teaches a method of desensitising a patient to a Der p I or a Der p II dust mite polypeptide allergen. Applicants disagree and traverse the rejection.

Claim 1 has now been amended to require that a late phase response occurs during desensitisation to the allergen. WO 94/21281 does not disclose use of a peptide as described in claim 1 with a specific patient in which a late phase response occurs as required by the amended claims. As discussed at page 7 line 30 to page 8 line 23 the late phase response occurs only in individuals who have been previously sensitised to allergen. In the absence of disclosure in WO 94/24281 of the combination of a peptide as described in claim 1 and a patient in whom the late phase response would occur, claim 1 is novel over this document. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

Hoyne et al.

The Office Action states that claims 1, 4-5 and 13 are rejected as anticipated by Hoyne et al. The Office Action states that Hoyne et al. teaches a method of desensitising a patient to a Der p I polypeptide allergen, wherein the peptide has a length of 20 amino acids and is not a Fel d I-derived peptide. Applicants disagree and traverse the rejection.

Hoyne *et al.*, does not teach the specific combination of providing a peptide according to claim 1 to an individual in whom a late phase response is stimulated by the

peptide. Therefore claim 1 is novel over this document. Further, claim 1 has now been limited to carrying out the method in humans. Hoyne et al. does not teach a method of providing a peptide to a human in whom a late phase response is stimulated. Accordingly, Hoyne et al. does not anticipate the claimed invention and Applicants request that the rejection be reconsidered and withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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